Examiner has requested that a choice be made for further prosecution. This choice is one of the following: (1) to have claim 1 allowed if amended to recite only SEQ ID NO:46; (2) to search 10 sequences if designated by Applicant; or (3) to have an Ex parte Quayle action issued indicating that claim 1 is allowable if amended to limit to SEQ ID NO:46 in the absence of further action by Applicant, thereby limiting prosecution.

Applicant elects (2), subject to the arguments below that suggest that the scope of allowable prosecution be broadened, and requests that the following sequences be examined: (1) SEQ ID NO: 46 (Q-R-A-N-L-R-A); (2) SEQ ID NO: 47 (T-S-H-G-L-T-T); (3) SEQ ID NO: 48 (R-S-D-T-L-S-N) (4) SEQ ID NO: 49 (T-T-G-N-L-T-11 V) (5) SEQ ID NO: 50 (S-P-A-D-L-T-R); (6) SEQ ID NO: 51 (D-K-K-D-L-T-R); (7) SEQ ID NO: 52 (R-T-D-T-L-R-D) (8) SEQ ID NO: 53 (T-H-L-D-L-I-R) (9) SEQ ID NO: 54 (Q-L-A-H-L-R-A); and (10) SEQ ID NO: 55 (R-S-D-H-L-A-E).

Applicant states that the sequences recited in originally filed claims 1-8 (SEQ ID NO: 7-70 and 107-112, should in fact be examined on the merits. The policy regarding examination of patent applications that claim large numbers of nucleotide sequences is set forth in 1192 O.G. 68 (November 19, 1996).

However, Applicant respectfully asserts that the provisions of that Official Gazette notice are inapplicable for at least the following reasons:

(1) Firstly, the Official Gazette notice is directed solely to claims that recite nucleotide sequences, not claims that recite peptide or polypeptide sequences. "Accordingly, in most cases, up to ten (10) independent and distinct nucleotide sequences will be examined in a single application without restriction." (1192 O.G. 68 (November 19, 1996), Section (II), ¶ 3) (emphasis added).

The claims at issue here are directed to polypeptides that incorporate defined heptapeptide or octapeptide zinc finger motifs. For example, claim 1 reads: "An

isolated polypeptide comprising from 2 to 12 zinc finger-nucleotide binding peptides at least one of which peptides contains a nucleotide binding region having the sequence of any of SEQ ID NO:7-70 and 107-112." This is clearly a claim to a polypeptide, not a nucleotide sequence or a combination of nucleotide sequences. Moreover, one aspect of the invention is that different zinc fingers (up to 12) can be combined in the same isolated polypeptide to yield a unique DNA-binding capacity to specific, desired sequences. This capacity provides a great degree of diversity in DNA binding, and this diversity is a significant part of the invention. Accordingly, the requirement for restriction that is being imposed means that Applicants are forced to abandon coverage of a substantial aspect of their invention.

The considerations for search of polypeptides are distinctly different than those for search of polynucleotides. For one thing, because of the degeneracy of the genetic code, there can be a large number of nucleotide sequences that encode the same polypeptide. If the claim specifies a polypeptide, not a polynucleotide, this is not an issue. For another, there are 20 naturally-occurring amino acids in polypeptides and only four naturally-occurring bases in polynucleotides. This means that the probability of chance matches is far lower for polypeptides than for polynucleotides and that regions of identity are more significant for polypeptides than for polynucleotides.

Because the Official Gazette notice emphasizes that the nucleotide sequences are to be considered as chemical compounds (1192 O.G. 68 (November 19, 1996), Section (II), ¶ 2), polypeptides, as chemical compounds, are completely distinct from polynucleotides. Their monomer building blocks and the linkages between the monomer units are completely distinct. This means that, adopting the approach of the Official Gazette notice itself, its provisions are inapplicable to polypeptide claims.

(2) Because the provisions of the Official Gazette notice are inapplicable to the claims at issue, the general principles governing restriction control. These principles mandate a broader examination of the claims on the merits.

The requirement to elect 10 sequences, treated as a requirement for the election of species, is respectfully traversed on the following grounds: Firstly, the Examiner has not met the required burden for demonstrating the necessity for election. M.P .E.P. § 803 requires for restriction, and by analogy for election, both (1) that the inventions are independent or distinct as claimed and (2) that there would exist a "serious burden" on the Examiner if all of the claims were examined together in one application.

These requirements have not been met. Firstly, there is no demonstration that a "serious burden" on the Examiner would exist.

The subject matter of the heptapeptide or octapeptide sequences recited within these claims is sufficiently interrelated that no serious burden on the Examiner would exist if all of the sequences were examined on the merits. This is because the art involved, if relevant art exists, largely overlaps. For example, publications describing nucleic acid sequences that encode proteins or peptides typically, given the state of the art, recite variant sequences at both the nucleic acid and the peptide level, typically produced by site-specific mutagenesis or another technique. This is done, as here, in an attempt to pinpoint the function of particular motifs or even particular residues in as detailed a manner as possible.

Therefore, a "serious burden" on the Examiner sufficient to require the election of species does not exist for these claims.

Secondly, the subject matter of the various alternatives within these claims, as claimed, is not distinct, but rather is related. This is because all of these inventions are substantially related by the activity of the heptapeptide or octapeptide sequences in directing the binding of specific nucleotide sequences by these zinc finger polypeptides. The existence of this common activity simplifies the search required and minimizes the burden on the Examiner, so that a "serious burden" does not exist.

Moreover, claim 1, quoted above, is a Markush-type claim claiming a number of species in the alternative. Restriction between the species recited in the alternative in a single claim is not appropriate unless the subject matter in that claim lacks unity of invention. In re Harnish, 206 U.S.P.Q. 300 (C.C.P.A. 1978); Ex parte Hozumi, 3 U.S.P.Q. 2d 1059 (Bd. Pat. App. & Int'f 1984). Unity of invention exists in a claim reciting species in the alternative, such as a Markush-type claim, where the species: (1) share a common utility; and (2) share a substantial structural feature disclosed as being essential to that utility. M.P.E.P. § 803.02; In re Haas, 179 U.S.P.Q. 623 (C.C.P.A. 1973) ("Haas I"); In re Haas, 198 U.S.P.Q. 324 (C.C.P.A. 1978) ("Haas II"); In re Weber, 198 U.S.P.Q. 328 (C.C.P.A. 1978). Applying this test, it is clear that unity of invention exists and restriction is therefore inappropriate. The polypeptides recited in claim 1 share a common utility, which is the sequence-specific binding of DNA by the zinc-finger moieties. The polypeptides also share a "substantial structural feature disclosed as being essential to that utility." That "substantial structural feature" is the zinc-finger motif itself, which is well-recognized in protein chemistry as a motif that confers specific nucleotide-sequence-binding capacity and has certain invariant structural features related to the amino acids that are directly involved in contacts with the bases of those nucleotides.

Applicant does not traverse the requirement to restrict to ten sequences, treated herein as a requirement for the election of species, on the basis of lack of patentable distinctness. Rather, Applicant traverses the requirement to restrict to ten sequences on basis of the relatedness of the subject matter of the inventions specified by various heptapeptide or octapeptide sequences, notwithstanding the possible existence of patentable distinctness. Applicant, who is presenting this information in a unitary manner in one patent application, should not be unduly penalized by a requirement to restrict to ten sequences when the subject matter of the inventions of these claims is so clearly related, particularly where, as here, a significant feature of the invention is the diversity of the sequence specificity attained.

More significantly, the art required to search all of these sequences is so closely related that there does not exist a "serious burden" on the Examiner if all of these inventions were searched and examined in a single application. The determination of the existence or non-existence of a "serious burden" should not be made according to arbitrary principles, but should reflect the actual state of the art.

The species of the invention recited in all of the pending claims are so closely related that there is no proper basis for requiring such an election between sequences. M.P.E.P. § 806.03 states: "Where the claims of an application define the same essential characteristics of a *single* disclosed embodiment of an invention, restriction therebetween should never be required. This is because the claims are but different definitions of the same disclosed subject matter, varying in breadth or scope of definition."

Here, all the claims are directed to isolated polypeptides that incorporate zinc finger heptapeptides or octapeptides and have the ability to bind specific trinucleotide sequences, specifically those with the residue adenine (A) at their 5′ end. The invention is based on a novel method for generating and analyzing such isolated peptides so that binding of specific trinucleotide sequences can be accomplished. Thus, the pending claims define the same essential characteristics of a single disclosed embodiment of the invention.

Treating the requirement for specifying ten peptide sequences as a requirement for election of species, Applicant does not traverse the requirement on the grounds of lack of patentable distinctness between the species. Rather, Applicant traverses the requirement on the grounds that the relatedness of the species precludes the requirement for election, notwithstanding possible patentable distinctness between the species.

Again, under the doctrine of In re Haas, 179 U.S.P.Q. 623 (C.C.P.A. 1973) ("Haas I"); In re Haas, 198 U.S.P.Q. 324 (C.C.P.A. 1978) ("Haas II"); In re Weber, 198 U.S.P.Q. 328 (C.C.P.A. 1978), followed by the United States Patent and Trademark Office, restriction of a single Markush-type claim is inappropriate where there is a common utility and a substantial structural feature responsible for that utility. Both of these elements are present here, making a requirement for election of a limited number of species within the scope of claim 1 inappropriate.

Accordingly, Applicant elects alternative (2) presented by the Examiner and makes the election of ten sequences as set forth in that alternative. However, Applicant also respectfully maintains that the requirement for the election of ten sequences does not comply with the general rules governing restriction and election and respectfully requests the Examiner to withdraw it.

If any issues remain, the Examiner is respectfully requested to telephone the undersigned at (858) 450-0099 x302.

Respectfully submitted,

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